

**Research Article**

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Maternal Diabetes Mellitus and Risk of Stillbirth: A Nested Case-Control Study in a Nigerian Tertiary Hospital

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Received Date: December 05, 2019**Published Date:** December 12, 2019**Abstract**

Background: Stillbirths have always been a contributor to psychological morbidity amongst women. Diabetes mellitus remains a significant risk factor for its occurrence. Knowledge of the causes and risk factors of this unfortunate problem will help in designing preventive measures to reduce its incidence.

Objective: To determine the relationship between maternal diabetes mellitus and the risk of stillbirths.

Methods: This is a nested case control study conducted in the Obstetrics unit of the Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria from 1st September 2014 to 31st August 2017. Forty-four women who had stillbirth were regarded as the cases and 44 women who had livebirths were regarded as the control group were retrieved from their case files. Information obtained included; type and sex of the stillborn, maternal age, type of stillbirth, parity, educational status, booking status, gestational age, and mode of delivery. Odds ratio (OR) with 95% confidence interval was calculated to determine the relationship between maternal diabetes and the risk of stillbirth.

Results: The risk of stillbirth in diabetic pregnancies irrespective of the type was found to be two times higher than in non-diabetic pregnancies (OR 2.16, 95% CI 0.72-6.30). The mean age of the women was found to be approximately 30 years in both cases and controls. The ratio of macerated stillbirth to fresh stillbirth was 1.4:1 and females were affected more than males in a ratio of 1.3:1. The mean gestational age at delivery was 35 weeks for the cases and 38 weeks for the control group. Majority of the women included in the cases had only a primary level of education (34.1%) and never accessed antenatal care services (79.5%) as against the majority of the women in the control group who had a tertiary level of education (45.5%) and were booked for antenatal care (72.7%).

Conclusion: This study established that there is a significant association between maternal diabetes mellitus and stillbirth. The increased occurrence in the cases could be due to ignorance, lack of antenatal care, low socioeconomic class and poor control of glycemic levels found among the women. Hence, the need for effective preventive/control programmes for these group of women.

Keywords: Stillbirths, Diabetes mellitus, Pregnancy

Introduction

The World Health Organization (WHO) defined stillbirth as the death of a fetus with a birth weight of at least 500g or if birth weight is unavailable [1,2], a gestational age beyond the age of viability. The stillbirth rate, as the perinatal mortality rate, is an important indicator of the quality of antenatal care and obstetric care during

labor and delivery [3]. Knowledge of the causes and risk factors of this unfortunate problem will help in designing preventive measures to reduce its incidence [4]. Stillbirths are common and devastating, and in developed countries, about one-third has been shown to be of unknown or unexplained origin [5]. Some

factors have been identified of which few of them have a direct causal relationship such as abruptio placentae, cord accidents, etc., while others may be indirectly related such as preeclampsia, maternal diabetes, maternal smoking, obstructed labor, maternal infections during pregnancy, etc. (all of which are modifiable factors). Stillbirth is classified as fresh stillbirth when the baby is born with an intact skin suggesting that the death occurs during labor (less than 12 hours before delivery), and macerated stillbirth, when there are signs of degeneration (peeling of skin, red serous effusions in the chest and abdomen due to Haemoglobin staining) suggesting that the death occurred more than 12-24 hours before labor [5]. Macerated stillbirths are often associated with insults that occur in utero during the antenatal period.

Diabetes concurrent with pregnancy is a high-risk condition and is associated with an increased risk of perinatal mortality [6-8] especially if poorly controlled. Other complications in the newborn include hypoglycemia, macrosomia, polycythemia, hyperbilirubinemia, respiratory distress syndrome, prematurity, shoulder dystocia, congenital anomalies, etc. [9-12].

Historically, diabetic pregnancies often ended in unexplained stillbirths [7]. Several researches and attempts have been made to identify the exact cause but has not yielded much results [9-12].

Globally, about 4% of all stillbirths remain attributable to diabetes and diabetic pregnancies continue to increase the risk for perinatal mortality [13]. Before the discovery of insulin, a woman with type 1 diabetes had almost no chance of successful delivery of a healthy baby [9]. With the advent of insulin treatment, pregnancy losses continued to be high, predominantly through stillbirths [9]. According to the WHO update, there were 2.6 million stillbirths in 2015 [10,11] accounting for over 7,178 deaths per day [11]. It has been noted that 98% of these deaths occur in the low- and middle-income populations [10]. About 66% of the worldwide stillbirths is contributed by the developing nations like India, Pakistan, Nigeria, China, Democratic Republic of Congo, Ethiopia, Bangladesh, Indonesia, Tanzania, and Afghanistan[1,2].

In this study, the authors hypothesized that there was no relationship between maternal diabetes and stillbirths (if odds ratio is <1). However, there has been extensive research into the effects of diabetes mellitus on pregnancy outcomes, and in particular on the risk of stillbirths [12,14-27] though not much work has been done in Africa and relatively none in Nigeria. This study was aimed at determining the relationship between maternal diabetes mellitus and the risk of stillbirths.

Methods

This research was carried out at the Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi. A nested case-control design was used to determine the relationship between maternal diabetes and the risk of stillbirth. The study population included the cases (all pregnant women who were admitted and delivered stillbirths whether fresh or macerated) and controls (pregnant women who

delivered live babies during the same period in the same hospital) of stillbirths that occurred from 1st September, 2014 to 31st August, 2017. Case files of women who carried their pregnancy beyond the age of viability (28 weeks) and delivered were included while case files of women who could not carry their pregnancy up to the age of viability were excluded. The data was gotten from the medical records department. Controls were randomly chosen in a ratio of 1:1 to the cases. Data extracted included the sex of the stillborn, maternal age, type of stillbirth, parity, educational status, booking status, gestational age (GA), glycemic levels. Maternal age and comorbidities were controlled to remove potential confounders. Data was analyzed and the odds ratio (OR) and 95% Confidence interval (95%CI) calculated to check for the statistical significance. This study was approved by the Ethics committee, NAUTH and permission obtained from the Head of Department, Medical Records, NAUTH, Nnewi before the patients' case files were retrieved. Information obtained were treated with utmost confidentiality.

Results

A total of 88 case files were analyzed during the study. The women (cases and controls) had their ages ranging from 21-42 years, with a mean age of 30.1 years and 20-38 age groups with a mean age of 29.6 years respectively. Up to 56.8% of the cases of stillbirths were females, while 43.2% were males giving a ratio of 1.3:1.

The types of stillbirth that occurred during the study period were also analyzed with 59.1% being macerated stillbirths (MSB) and 40.9% being fresh stillbirths (FSB) giving a ratio of 1.4:1. The parity of the women included in the cases were analyzed, with 79.5% being multiparous, 13.6% primiparous and 6.8% grand multiparous. Up to 38.7% of the women had a primary level of education, 34.1% secondary and 27.3% tertiary level. Majority of the women included in the cases were unbooked (79.5%). Considering the mode of delivery, 68.2% of the women had vaginal delivery while the remainder delivered via Caesarean section (31.8%). The mean gestational age at delivery in the cases was found to be 35.3 weeks.

The parity of the women included in the controls were analyzed, with 52.3% being multiparous, 43.2% primiparous and 4.5% grand multiparous. Up to 36.4% of the women had a secondary level of education, 45.5% tertiary level while 18.1% stopped at primary level. A majority of the women were booked (72.7%). Considering the mode of delivery, 61.4% of the women had vaginal delivery while the remainder delivered via caesarean section (38.6%). The mean gestational age at delivery for the controls was 38.0 weeks.

Using a 1:1 matching criterion, 44 of them were the cases and 44 were the controls. The 44 cases were those that met the inclusion criteria and were included in the study. The odds ratio revealed a statistically significant association between diabetes mellitus and the occurrence of stillbirths (OR 2.16, 95% CI 0.72-6.30) (Tables 1&2).

Table 1: Socio-demographic characteristics of the study population.

Cases		Controls	
Characteristics	Mean (years)	Characteristics	Mean (years)
Age (years)		Age (years)	
21 – 42	30.1	20 – 38	29.6
Frequency (%)			
[N=44]			
Sex of stillbirths			
Male	19(43.2)		
Female	25(56.8)		
Type of stillbirths			
MSB	26(59.1)		
FSB	18(40.9)		
Parity		Parity	
Primipara(1)	6(13.6)	Primipara(1)	19(43.2)
Multipara(2-4)	35(79.5)	Multipara(2-4)	23(52.3)
Grand Multipara(>5)	3(6.8)	Grand Multipara (>5)	2(4.5)
Educational level		Educational level	
Primary	17(38.7)	Primary	8(18.1)
Secondary	15(34.1)	Secondary	16(36.4)
Tertiary	12(27.3)	Tertiary	20(45.5)
Booking status		Booking status	
Booked	9(20.5)	Booked	32(72.7)
Unbooked	35(79.5)	Unbooked	12(27.3)
Mode of delivery		Mode of delivery	
VD	30(68.2)	VD	27(61.4)
C/S	14(31.8)	C/S	17(38.6)
Mean(weeks)		Mean (weeks)	
GA at delivery (weeks)	35.3	GA at delivery (weeks)	38
28 – 42		31 – 42	

Abbreviations: MSB= Macerated Stillbirth; FSB= Fresh Stillbirth; VD= Vaginal Delivery; C/S= Caesarean Section; GA= Gestational Age

Table 2: Maternal diabetes mellitus and the risk of stillbirth.

	Cases (Stillbirths)	Controls (live births)	Total
Mothers with diabetes mellitus during pregnancy	6	3	9
Mothers without diabetes mellitus during pregnancy	38	41	78
Total	44	44	88
Odds ratio: (OR 2.16, 95% CI 0.72-6.30)			

Discussion

This study confirmed a statistically significant relationship between maternal diabetes mellitus and the risk of stillbirths (OR 2.16, 95% CI 0.72-6.30). This means that women with diabetes mellitus during pregnancy were two times more likely to have a stillbirth when compared to the general population which agreed with a similar study done in different parts of the world by Tennant,

et al., Stringer, et al., Hogue et al., and Schmidt, et al. [18,20,24,26].

The mean age of the cases was 30.14 years while those of the control group were 29.6 years. Low socioeconomic levels contributed to the occurrence of stillbirth amongst the women who were included in the cases as evidenced by the sharp contrast between the two groups – cases (majority had only a secondary level of education) and controls (majority had a tertiary level of education). This was in concordance with a study done by Lyon, et al. [32]. In this study, 40.9% were fresh stillbirths (FSB) and 50.9% were macerated stillbirths (MSB). Alrahman and Alaf, and Di Mario et al found that two thirds to three quarters of stillbirths occurred before labor which are often associated with insults that occurred during the antenatal period [27,28].

This study reported a ratio of 1.4:1 between MSB and FSB. There was a slight increased rate of affectation of the females when compared to the males in a ratio of 1.3:1 which disagreed with a similar study conducted by Petridon, et al. and Alrahman and Alaf who found higher mortality rate among male fetuses [28,30]. On comparison of the booking status of the cases (booked 20.5%, unbooked 79.5%) and controls (booked 72.7%, unbooked 27.3%), it was found that women who booked for antenatal care during pregnancy had a significantly decreased risk of having stillbirths due to proper monitoring of the progress of pregnancy during the antenatal period which included good glycemic control in those of them who had diabetes mellitus. This correlated with a similar study done by Alrahman and Alaf, Agudelo, et al. and Feresus, et al. [28-31].

Majority of the women who had stillbirths had vaginal delivery, 65.9%, while the rest delivered via caesarean section, 31.8%. This agreed with a similar study done in Erbil Teaching Hospital, Kurdistan region, Iraq [28]. On analysis of the mean gestational age in both cases (35.3weeks) and controls (38.0weeks), it was also found that mothers included in the cases delivered pre-term (<37 completed weeks). Also, noted in the pregnancy outcomes in women who had diabetes mellitus included omphalocele, fetal macrosomia, congenital hip dislocation in some of the babies delivered and polyhydramions in their mothers during pregnancy.

The major strength of this study is the nested case-control of its design. It appears to be the first case-control study in the study center on the potential relationships between diabetes mellitus and still birth rates. The major limitations were that some data were missed due to the fact that data were retrospectively extracted in the case files. Further study will require a prospective design.

Conclusion

This study established that there is a significant association between maternal diabetes mellitus and stillbirth. The increased occurrence in the cases could be due to ignorance, lack of antenatal care, low socioeconomic class and poor control of glycemic levels found among the women. Hence, the need for effective preventive/control programmes for these group of women. There is also the need for adequate and close monitoring of the glycemic levels of those diabetic prior to conception or at risk of developing diabetes

mellitus during pregnancy. Also, monitoring of the fetal kick counts and symphysio-fundal height measurement are very essential and would help detect the early signs of hypoxia in the fetus.

Authors Contribution

JUE and IBU contributed to the study conceptualization and methodology; JUE conducted the clinic study, ensured completion of the participants data and extracted the required data; JUE and GUE analysed the data and drafted the original manuscript; EAE and OSU worked with JUE on formal analysis; IBU, GUE, EOU, EAE and OSU contributed to the project administration, writing (review and editing), data visualization, and supervision. All authors have seen and approved their contributions and the final version of the manuscript.

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Conflict of Interest

Authors declare no conflict of interest.

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